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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/580,704	05/30/2000	George Peter Lomonossoff	DOW-04647	2167

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MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

3/21/05 RA

Office Action Summary	Application No.	Applicant(s)	
	09/580,704	LOMONOSSOFF ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a response, filed 12/23/2004, amending claims 1 and 9. Claims 1, 4-9 and 12-16 are currently pending and under consideration in this action. All objections/rejections not repeated herein are hereby withdrawn. A response to Applicant's arguments will be set forth, where applicable, in the body of any rejection maintained. Because new grounds of rejection are set forth, this action is non-final.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

1. **Claims 1 and 4-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

As amended, base claim 1 is directed to a plant infected with a modified virus. The claim recites the phrase, "animal virus *inserted into plant viral genomic nucleic acid that codes for an expressed native portion of the plant viral coat protein*, said inserted nucleotide sequences being an addition to the existing native functional plant viral nucleic acid". (emphasis added). Attention is directed to the emphasized portion of the claim, which is the source of vagueness and indefinite boundaries. The claim is vague and indefinite, because it is unclear whether the inserted animal virus nucleic acid is being inserted into a plant viral nucleic acid that encodes a coat protein of said plant virus or merely being inserted anywhere in the plant virus genome.

More particularly, the source of the ambiguity is the term "genomic", because either the insertion is inserted into a particular plant virus nucleic acid that encodes a coat protein or inserted *anywhere* in the viral genomic nucleic acid, where the viral nucleic acid encodes a coat protein(s) as well as other proteins. If the former interpretation is adopted, then the insertion is in any plant viral nucleic acid that encodes a native plant virus coat protein; If the latter interpretation is adopted, then the insertion is anywhere in the entire plant viral genome and not necessarily limited to regions that encode a plant virus native coat protein. It would be remedial to replace the cited phrase, with a phrase that more distinctly and particularly recites that Applicant intends, i.e., insertion into the plant virus nucleic acid that encodes a coat protein from said plant virus. Alternatively, the phrase can be replaced with a phrase directed to an insertion into the plant virus genomic nucleic acid so as to encode a fusion protein with the plant virus coat protein. However, as written, the claim is vague and indefinite.

Furthermore, as written the claim is vague as to whether the insertion of the foreign peptide is the "modification" or whether some other undefined modification is necessary. It is understood from the full disclosure that the insertion is the modification claimed (e.g., claim 9, subpart *b*). Therefore, as written the claim is ambiguous, thus the claims' metes and bounds are indeterminable.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Claims 1, 4-9 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.**

This is a new ground of rejection. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. More particularly, the subject matter in question is directed to inserting a nucleotide sequence encoding an animal virus in any site, of any plant viral nucleic acid encoding viral coat protein, wherein the peptide can be of any size.

The test for enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the specification coupled with information known in the art without undue experimentation. *United States v Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor but instead is a conclusion reached by weighing many factors which are outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). The factors include the following:

Scope/Breadth of the claims.

The claims are broad in scope and breadth. Base claims 1 and 9 are directed to infected plants or methods of producing modified plant viruses from infected plants, wherein *any* plant virus is modified by insertion of nucleic acid encoding an animal virus peptide of *any* size, at *any* site within the viral genome or inserting at the "part of said plant viral genome that codes for an expressed native portion of the viral coat protein". Additional claims are directed to any plant virus that is an RNA virus and any modified comovirus.

However, the dependent claims are still broad insofar as being directed to any RNA virus, or inserting any sized nucleic acid in any RNA virus or in any comovirus, or insertion anywhere in the RNA or comovirus genome, or insertion anywhere in the RNA virus or comovirus nucleic acid that encodes for said virus coat protein(s).

Nature of the invention.

The invention is directed to products and methods for antigen or peptide presentation, where a modified plant virus expresses coat proteins with the foreign peptide and infects the host plant so as to produce an appreciable quantity of assembled modified viral particles expressing said fusion proteins.

State of the art/Unpredictability of the art.

The art of antigen presentation is generally known in the prior art. However, each vectors/host cells that are utilized to facilitate antigen presentation on whole define the particular antigen presentation products/methods. More particularly, with respect to plant viruses that are infections and express a foreign peptide, there is unpredictability as to the size of the peptide being expressed, the sequence of the peptide being expressed, the particular virus that is being used and the site of insertion for the foreign nucleic acid.

For example, with respect to the cowpea mosaic virus (CPMV) it is not known whether the size of the insert can affect assembly/expression or infection of the host plant. (e.g., Porta et al. Virology. 1994; 202:949-55; p. 954, col. 2, ¶ 2). Therefore, depending on the size of a particular insert, there could be deleterious effects on virus growth or infectivity, thus obviating plant infection or production of viral particles as claimed.

Furthermore, insertion of foreign nucleic acids is limited to particular regions that encode particular coat proteins. For example, if insertion is made in a nonoptimal position in the βB-βC loop of the S [coat] protein, plant virus infection is limited to localized lesions, reducing production and infectivity. (Id., col. 1). Therefore, even for a single plant viral species (i.e., CPMV), insertion of a foreign peptide is limited to very precise locations in the coat protein, thus insertion in other coat protein-encoding regions would impart unpredictability. Such a level of unpredictability would be amplified more so if the particular plant virus genome/particle is uncharacterized or for which the three dimensional structure is unknown. (e.g., Brennan et al. Mol. Biotech. 2001; 17:15-26, p. 16, col. 1, § 2.1; teaching that potential sites for insertion of foreign sequences were determined by examining the three dimensional structure of CPMV). As Applicant's have disclosed in the instant disclosure, with respect to CPMV the specific site of insertion is the βB-βC loop of the *S* protein, as this is the only site that likely allows for expression without disrupting viral capsid protein-protein interactions that can preclude viral assembly and infectivity.

All plant viruses or RNA viruses are not interchangeable with respect to expression of foreign peptides and plant infectivity/ viral propagation. For example, once a potential site is identified, depending on a particular plant virus, replacement may facilitate presentation, while in others insertion and expression as fusions in addition to native coat protein is to only successful means of expression or infectivity. (e.g., Takamatsu et al. FEBS letters. 1990; 269: 73-6; teaching replacement of tobacco mosaic virus (TMV) coat protein with a marker protein and successful expression; Usha et al. 1993. Virology; 197:366-74; teaching that since removal of wild-type sequences abolishes infectivity, foreign sequences are expressed in addition to

rather as replacements, at a position immediately adjacent to praline 23). Therefore, knowledge in the art suggests that all plant RNA viruses are not equivalents or interchangeable with respect to antigen presentation.

Furthermore, even where the system is limited only to CPMV, the sequence of the particular foreign peptide may affect expression and infectivity, thus exacerbating unpredictability. For example, if the particular insert contains sequences that are involved cell attachment, the expression foreign peptide encoding an animal virus peptide may actually result in immobilization of the assembled viral particle, resulting in loss of infectivity, which in turn means no plant infection or no viral particle production. For example, if the foreign peptide contains an Arg-Gly-Asp motif, expression as a chimera with CPMV *S* protein may result in particle immobilization, hence no infection/production. (Supra, Porta et al. 1994. p. 954, col. 2; teaching that sequences encoding foreign peptides from foot and mouth disease virus in a CPMV antigen presentation system resulted in immobilization of the viral particle thus precluding infection). In sum, the knowledge in the art teaches that insertion of any insert, anywhere in the genome of any plant virus, or any RNA virus, or anywhere within regions encoding coat proteins for the same, is unpredictable.

Amount of guidance provided.

The specification provides that viruses that encode capsid proteins containing separate moieties from that which codes for other functional molecules and whose coat proteins have a β-barrel structure are particularly useful as vectors in antigen presentation.

Further, the specification provides that comoviruses have an advantage of containing sixty copies each of 3 different β-barrels, which can be individually manipulated. (Specification, pp. 4, bottom, bridging to p. 5 top; p. 9, bottom bridging to p. 10 top). No other substantial guidance is provided as to insertion of foreign sequences anywhere or in any other plant or RNA virus. No discussion or guidance is provided as to unpredictability of results that can arise depending on the size or sequence of a particular insert. In addition, no substantial relevant guidance is provided in regard to insertion into other nucleic acid regions of CPMV that encode other proteins or other coat proteins.

Number of working examples.

A single example is presented, insofar as teaching a plant virus, the coat protein of which can be modified by insertion of a foreign animal virus peptide. More specifically, the specification discloses CPMV that has been modified with three distinct insertions, but where all the insertions are into the βB-βC loop of the S coat protein. No other examples of other plant viruses, other comoviruses other RNA viruses or of insertion into any other portion of the CPMV genome is disclosed.

Amount of Experimentation Required.

The level of skill in the art required to practice the claimed invention is high. Given the unsolved hurdles to successful practicing of the invention, the level of unpredictability in the art and lack of a sufficient number of relevant working examples, it must be considered that the skilled artisan would be required to conduct trial and error experimentation of an undue nature in order to attempt to practice the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.
See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. **Claims 9 and 12-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 5,874,087.**

This rejection was made previously. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 9 and 12-16 are drawn to a genus of a method of producing a modified plant virus, while reference claims 1-9 are drawn to a species of a method of producing a modified plant virus. Species claims necessarily make obvious the broader genus claims.

4. **Claims 9 and 12-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-28 of U.S. Patent No. 5,958,422.**

This rejection was made previously. The same analysis as above applies here. The genus claims are necessarily made obvious by the species claims.

Response to Arguments

No arguments have been presented with respect to the Double Patenting rejections.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Ray Akhavan
AU 1636

GERRY LEFFERS
PRIMARY EXAMINER